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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,843	04/08/2005	Susanne Leonhartsberger	LEONHARTSBERGER	3626

25889 7590 02/28/2007

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	PAPER NUMBER
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,843	LEONHARTSBERGER ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/9/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *CRF- error report*.

DETAILED ACTION

1. Applicants' Preliminary Amendment filed November 18, 2005 is acknowledged. Claims 1-8 are pending and under consideration in this examination.

2. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an application filed in Germany on 10.22.2002.

3. ***Drawings***

This application has been filed with drawing (Figure 1), which is acceptable for examination purposes only.

Figure 1, however, is not described in the specification. Applicants are required to amend the specification to include a 'Brief description of the drawing'.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.

(b) CROSS-REFERENCE TO RELATED APPLICATIONS.

(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.

(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.

(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.

(f) BACKGROUND OF THE INVENTION.

(1) Field of the Invention.

(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.

(g) BRIEF SUMMARY OF THE INVENTION.

(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).

(i) DETAILED DESCRIPTION OF THE INVENTION.

(j) CLAIM OR CLAIMS (commencing on a separate sheet).

(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).

(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

4. ***Sequence Rules***

The instant specification present amino acid and nucleic acid sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), but fails to comply with the requirements of 37 CFR 1.821-825. While every disclosed amino acid sequence of four or more residues or 10 or more nucleotides have been identified by a SEQ ID NO:, the CRF submission is flawed.

Applicant must submit a CRF copy and paper copy of the Sequence Listing, a statement that the content of the paper and computer readable copies are the same and where applicable

include no new matter as required by 37 C.F.R. j 1.821(e) or 1.821(9 or 1.821(g) or 1 .825(d), as well as an amendment directing its entry into the specification.

New Sequence Rules

Since the effective filing date after July 1, 1998, Applicants should follow the New Rule Format and submit a new Sequence Listing (both in electronic and paper format). Compliance according to the requirements of 37 CFR 1.821 through 1.825 is required.

Note- Applicants have in the past made several attempts to comply with the sequence rules. However, these attempts were unsuccessful because the CRF IS FLAWED TECHNICALLY / NOT ENTERED INTO DATABASE. A copy of the Raw sequence listing error report generated by the STIC Biotechnology Systems Branch of the USPTO is enclosed. Compliance with the sequence rules is required.

5. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

6. Claim 3 objected to because of the following informalities: Claim 3 refers to mutations listed in Table 1. Table 1 presents plasmids containing mutated and non-mutated forms of MetA. To simplify the claimed subject matter Applicants are suggested define the mutants in the claims. Perhaps using Markush language--- wherein the mutation is selected from Asp101Asn, Asp101His, Asp101Cys, Asp101Ser, Asp101Tyr, Asp101Ala, Asp101Ile; Tyr294Cys, Tyr294Leu, Tyr294Ala, Tyr294Pro, Tyr294Gln, Tyr294Lys or wherein Tyr294 is deleted. Instead of referring to the Table it is suggested to claim the limited

number of mutations by listing all the mutants in the manner suggested above. Appropriate correction is suggested.

7. ***Claim Rejections - 35 USC § 112*** (first paragraph)

Deposit Requirement

Claims 6-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the [plasmid/microorganism/vector] is required to practice the claimed invention. As such the [plasmid/microorganism/vector] must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the [plasmid/microorganism/vector]. The specification lacks complete deposit information for the deposit of [plasmid/microorganism/vector]. If a deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing

that (a) during pendency of the application, access to the invention will be afforded to the Commissioner upon request, (b) all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, (c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, (d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807) and (e) the deposit will be replaced if it should ever become inviable.

Claims 6-8 require the use of 'a microbial strain' to practice the claimed invention. It is not clear which strain is required and if a deposit is made as the criteria set forth in 37 CFR 1.801-1.809. In case Applicants' intentions are to claim 'host cell', Applicants may amend claims 6-8 to recite 'An isolated microbial host cell' to overcome this rejection.

Claims 6-8 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

EFFECTIVE MARCH 23, 1998 : New address for ATCC deposits.
AMERICAN TYPE CULTURE COLLECTION
10801 University Boulevard, Manassas, VA 20110-2209

8. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 1-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 1 is drawn to specific mutation corresponding to specific position of a sequence. However, there is no corresponding sequence or reference sequence present in the

claim. The instant specification, page 4, indicated the reference sequence of the wild-type homoserine transsuccinylase to be SEQ ID NO: 2. Addition of SEQ ID NO: 2 as the corresponding reference sequence to claim 1 will overcome this rejection.

Claims 2-8 are included in the rejection for failing to correct the defect in the rejected base claim.

9. Claims 6-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-8 require the use of 'a microbial strain' to practice the claimed invention. It is not clear which strain is required. In case Applicants' intentions are to claim 'host cell', Applicants may amend claims 6-8 to recite 'An isolated microbial host cell' to overcome this rejection.

10. ***Written Description***

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 1-8 (directly or indirectly) recite 'A mutant homoserine transsuccinylase or a MetA allele (or DNA) encoding the mutant homoserine transsuccinylase with specific amino acid residues modifications, plasmid and host cell (microorganism strain) comprising the MetA allele (or DNA). However, description to the reference homoserine transsuccinylase sequence of SEQ ID NO: 2 is lacking.

The specification, however, only provides the reference sequence of a single (single species) homoserine transsuccinylase sequence of SEQ ID NO: 2. The specification does teach a uniform numbering system of a specific SEQ ID NO:? other than SEQ ID NO: 2, that can be followed to mutate positions 101 or 294 with respect to homoserine transsuccinylase from any source, in order to exhibit reduced sensitivity towards L-methionine or SAM, the genus claimed. Description of single species is insufficient to describe the claimed genus.

The specification therefore fails to describe additional representative species of these homoserine transsuccinylase by any identifying structural characteristics other than by name recited in claims, for which no predictability of structure is apparent. Given this lack of structure of the sequence(s) of the homoserine transsuccinylase or the encoding DNA or MetA allele, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention. Therefore, the written description requirement is not satisfied.

11. ***Enablement Rejection***

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated mutant of homoserine transsuccinylase of SEQ ID NO: 2 (from *E. coli*) selected from a group consisting of Asp101Asn, Asp101His, Asp101Cys, Asp101Ser, Asp101Tyr, Asp101Ala, Asp101Ile; Tyr294Cys, Tyr294Leu, Tyr294Ala, Tyr294Pro, Tyr294Gln, Tyr294Lys or wherein Tyr294 is deleted, the encoding DNA, vector and isolated microbial host cell, wherein the mutants exhibit reduced sensitivity towards L-methionine or S-

adenosyl methionine (SAM), does not reasonably provide enablement for any homoserine transsuccinylase wild-type enzyme, wherein the wild type enzyme possessing an amino acid sequence which comprises a constituent sequence AspGlyXaaXaaXaaThrGlyAlaPro between positions 90-115 and a constituent sequence TyrGlnXaaThrPro between positions 285 and 310, wherein the mutation is an amino acid replacement of the Aspartate in the constituent sequence AspGlyXaaXaaXaaThrGlyAlaPro or an amino acid replacement in the constituent sequence TyrGlnXaaThrPro.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide sequence and encoded amino acid sequence of SEQ ID NO: 2, and wherein the amino acid sequence is specifically modified at a position selected from the following mutations - Asp101Asn, Asp101His,

Asp101Cys, Asp101Ser, Asp101Tyr, Asp101Ala, Asp101Ile; Tyr294Cys, Tyr294Leu, Tyr294Ala, Tyr294Pro, Tyr294Gln, Tyr294Lys or wherein Tyr294 is deleted.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications including the specific ones and with respect to any homoserine transsuccinylase wild-type enzyme from any source and have constituent amino acid sequence inserts AspGlyXaaXaaXaaThrGlyAlaPro or TyrGlnXaaThrPro at selected positions, because the specification does **not** establish: (A) regions of the any homoserine transsuccinylase structure which may be modified without effecting the mutants exhibiting reduced sensitivity towards L-methionine or S-adenosyl methionine (SAM); (B) the general tolerance of homoserine transsuccinylase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any homoserine transsuccinylase enzyme residues with an expectation of obtaining the desired enzymatic or biological function capable of exhibiting reduced sensitivity towards L-methionine or S-adenosyl methionine (SAM); and (D) the

specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus there is high unpredictability associated with respect to modification(s) of the any of the homoserine transsuccinylase sequences and from any source unless guidance is provided in establishing (A) - (D) as discussed above.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature of the mutant homoserine transsuccinylase, DNA (or polynucleotide) encoding a specific mutant homoserine transsuccinylase enzyme from any source and having the desired enzymatic characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

12. **35 U.S.C. § 101**

35 U.S.C. § 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 4-5 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims 4-5 as follows - (1) "isolated nucleic acid encoding homoserine transsuccinylase (or homoserine succinyltransferase)" for claim 4, and (3) "A plasmid transformed with isolated nucleic acid encoding homoserine transsuccinylase (or homoserine succinyltransferase)" for claim 5.

13. ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(a) Claims 1-8 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-8 of copending **Application No. 10/530844.**

This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: The claims in the two application are drawn to same subject matter. The instant claims anticipate the claims of the pending application.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on

access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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